

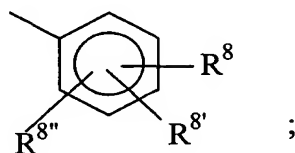
(IV)

wherein

$R^1$  is lower alkyl, aryl or arylalkyl;

$R^2$  is hydrogen, hydroxy, alkoxy,  $-\text{CH}_2\text{OH}$ , cyano,  $-\text{C}(\text{O})\text{OR}^7$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{CONH}_2$ , tetrazole,  $-\text{CH}_2\text{NH}_2$  or halogen;

$R^3$  is hydrogen, alkyl, heterocycle or



$R^4$  is hydrogen, alkyl or B;

$R^5$ ,  $R^{5'}$ ,  $R^8$ ,  $R^{8'}$  and  $R^{8''}$  are independently hydrogen, alkoxy, lower alkyl, halogen,  $-\text{OH}$ ,  $-\text{CN}$ ,  $-(\text{CH}_2)_n\text{NR}^6\text{COR}^7$ ,  $-\text{CON}(\text{R}^6)\text{R}^6$ ,  $-\text{CON}(\text{R}^6)\text{OR}^6$ ,  $-\text{CO}_2\text{R}^6$ ,  $-\text{SR}^7$ ,  $-\text{SOR}^7$ ,  $-\text{SO}_2\text{R}^7$ ,  $-\text{N}(\text{R}^6)\text{SO}_2\text{R}^1$ ,  $-\text{N}(\text{R}^6)\text{R}^6$ ,  $-\text{NR}^6\text{COR}^7$ ,  $-\text{OCH}_2\text{CON}(\text{R}^6)\text{R}^6$ ,  $-\text{OCH}_2\text{CO}_2\text{R}^7$  or aryl; or

$R^5$  and  $R^{5'}$  or  $R^8$  and  $R^{8'}$  may together with the carbon atoms to which they are attached form an aryl or heterocycle;

$R^6$  and  $R^{6'}$  are independently hydrogen or lower alkyl; and

$R^7$  is lower alkyl;

$R^9$  and  $R^{9'}$  are independently hydrogen, lower alkyl, alkyl, cycloalkyl, arylalkyl, aryl, heteroaryl; or

$R^9$  and  $R^{9'}$  may together with the nitrogen atom to which they are attached form a heterocycle;

A is a bond,  $-(\text{CH}_2)_n-$  or  $-\text{CH}(\text{B})-$ , wherein n is an integer of 1, 2 or 3 and

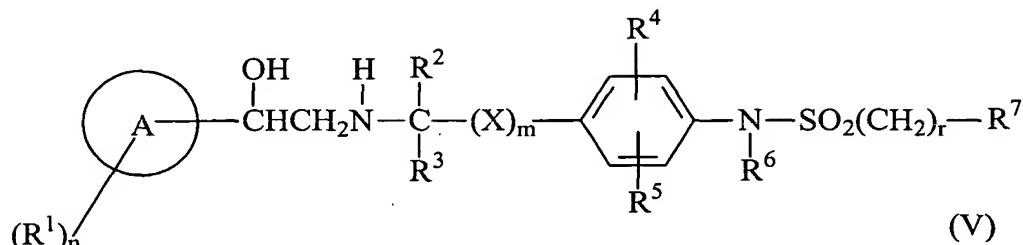
B is  $-\text{CN}$ ,  $-\text{CON}(\text{R}^9)\text{R}^{9'}$  or  $-\text{CO}_2\text{R}^7$ ;

with the proviso that when A is a bond or  $-(\text{CH}_2)_n-$  and  $R^3$  is hydrogen or

unsubstituted alkyl, then  $R^4$  is B or substituted alkyl;

(b) a compound of formula (V) is represented by the following general formula:

wherein



$n$  is 0 to 5;

$m$  is 0 or 1;

$r$  is 0 to 3;

A is pyridinyl;

$R^1$  is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5)  $NR^8R^8$ , (6)  $SR^8$ , (7) trifluoromethyl, (8)  $C_1$ - $C_{10}$  alkyl, (9)  $OR^8$ , (10)  $SO_2R^9$ , (11)  $OCOR^9$ , (12)  $NR^8COR^9$ , (13)  $COR^9$ , (14)  $NR^8SO_2R^9$ , (15)  $NR^8CO_2R^8$ , or (16)  $C_1$ - $C_{10}$  alkyl substituted by hydroxy, halogen, cyano,  $NR^8R^8$ ,  $SR^8$ , trifluoromethyl,  $OR^8$ ,  $C_3$ - $C_8$  cycloalkyl, phenyl,  $NR^8COR^9$ ,  $COR^9$ ,  $SO_2R^9$ ,  $OCOR^9$ ,  $NR^8SO_2R^9$  or  $NR^8CO_2R^8$ ;

$R^2$  and  $R^3$  are independently (1) hydrogen, (2)  $C_1$ - $C_{10}$  alkyl or (3)  $C_1$ - $C_{10}$  alkyl with 1 to 4 substituents selected from hydroxy,  $C_1$ - $C_{10}$  alkoxy, or halogen;

X is (1)  $-CH_2-$ , (2)  $-CH_2-CH_2-$ , (3)  $-CH=CH-$  or (4)  $-CH_2O-$ ;

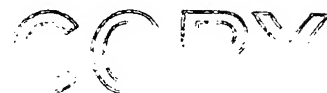
$R^4$  and  $R^5$  are independently (1) hydrogen, (2)  $C_1$ - $C_{10}$  alkyl, (3) halogen, (4)  $NHR^8$ , (5)  $OR^8$ , (6)  $SO_2R^9$  or (7)  $NHSO_2R^9$ ;

$R^6$  is (1) hydrogen or (2)  $C_1$ - $C_{10}$  alkyl;

$R^7$  is  $Z-(R^{1a})_n$ ;

$R^{1a}$  is (1)  $R^1$ , (2)  $C_3$ - $C_8$  cycloalkyl, (3) phenyl optionally substituted with up to 4 groups independently selected from  $R^8$ ,  $NR^8R^8$ ,  $OR^8$ ,  $SR^8$  or halogen, or (4) 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, optionally substituted with up to four groups independently selected from oxo,  $R^8$ ,  $NR^8R^8$ ,  $OR^8$ ,  $SR^8$ , or halogen;

Z is (1) phenyl, (2) naphthyl, (3) or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (4) a benzene ring fused to a  $C_3$ - $C_8$



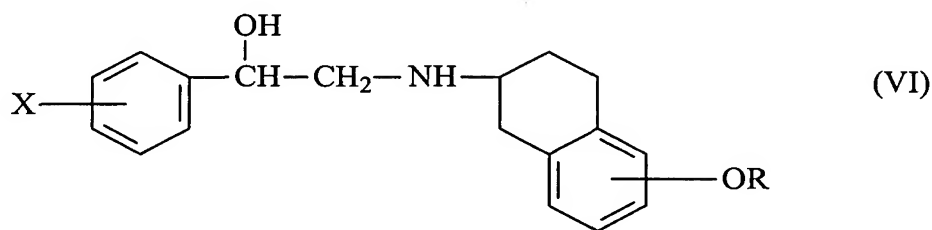
cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a C<sub>3</sub>-C<sub>8</sub> cycloalkyl ring;

R<sup>8</sup> is (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub>alkyl, (3) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (4) Z optionally having 1 to 4 substituents selected from halogen, nitro, oxo, NR<sup>10</sup>R<sup>10</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>1</sub>-C<sub>10</sub> alkylthio, and C<sub>1</sub>-C<sub>10</sub> alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, SO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, or Z optionally substituted by from 1 to 3 halogen, C<sub>1</sub>-C<sub>10</sub> alkyl or C<sub>1</sub>-C<sub>10</sub> alkoxy, or (5) C<sub>1</sub>-C<sub>10</sub> alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, SO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>1</sub>-C<sub>10</sub> alkyl, or Z optionally substituted by from 1 to 4 halogen, C<sub>1</sub>-C<sub>10</sub> alkyl or C<sub>1</sub>-C<sub>10</sub> alkoxy;

R<sup>9</sup> is (1) R<sup>8</sup> or (2) NR<sup>8</sup>R<sup>8</sup>; and

R<sup>10</sup> is (1) C<sub>1</sub>-C<sub>10</sub> alkyl, or (2) two R<sup>10</sup> groups together with the N to which they are attached forming a 5 or 6-membered ring optionally substituted with C<sub>1</sub>-C<sub>10</sub> alkyl;

(c) a compound of formula (VI) is:

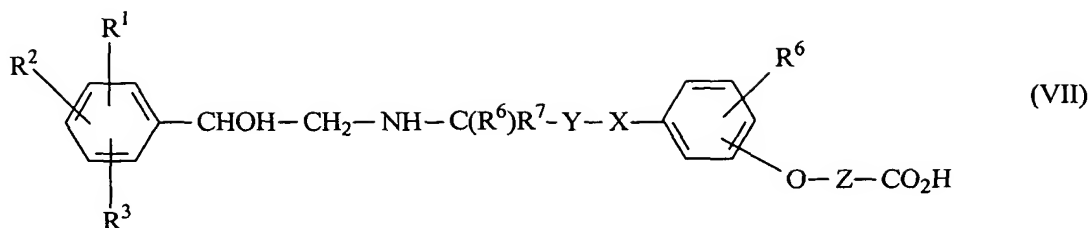


wherein

X is hydrogen, halogen, trifluoromethyl or lower alkyl, and

R is hydrogen; lower alkyl which may have a suitable substituent selected from the group consisting of cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl, hydroxy, lower alkoxy, carboxy and lower alkoxy carbonyl; cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl or lower alkanoyl;

(d) a compound of formula (VII) is represented by the following general formula:



wherein

R<sup>1</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or *p*-methoxybenzylamino group;

R<sup>2</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group;

R<sup>3</sup> is a hydrogen, chlorine or bromine atom or a hydroxyl group,

R<sup>4</sup> is a hydrogen atom or a methyl group;

R<sup>5</sup> is a hydrogen atom or a methyl group;

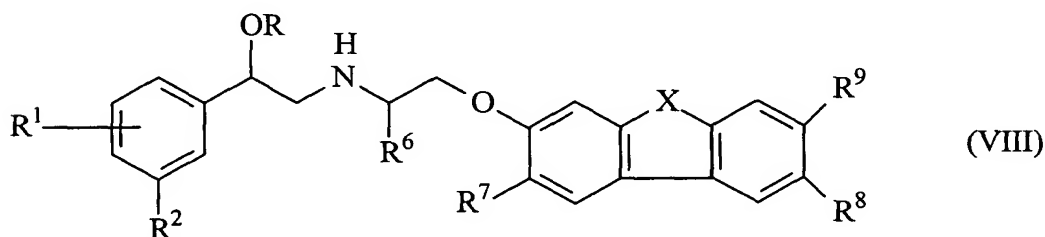
R<sup>6</sup> is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group;

X is an oxygen atom or a bond;

Y is an alkylene group of up to 6 carbon atoms or a bond; and

Z is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms; and

(e) a compound of formula (VIII) is represented by the following general formula:



wherein

R is hydrogen or methyl,

R<sup>1</sup> is hydrogen, halogen, hydroxy, benzyloxy, amino or hydroxymethyl,

R<sup>2</sup> is hydrogen, hydroxymethyl, -NHR<sup>3</sup>, -SO<sub>2</sub>NR<sup>4</sup>R<sup>4'</sup> or nitro,

R<sup>3</sup> is hydrogen, methyl, -SO<sub>2</sub>R<sup>5</sup>, formyl or -CONHR<sup>6</sup>,

R<sup>4</sup> and R<sup>4'</sup> are independently hydrogen, lower alkyl or benzyl,

R<sup>5</sup> is lower alkyl, benzyl or -NR<sup>4</sup>R<sup>4'</sup>,

$R^6$  is hydrogen or lower alkyl,  
 $R^6$  is hydrogen or lower alkyl,  
 $R^9$  is hydrogen, amino, acetylamino or hydroxy, and  
X is N, O, S or methylene;  
provided that when X is N, O or S,  
then  $R^9$  is hydrogen, either  $R^7$  or  $R^8$  is hydrogen, and the other is hydrogen, amino,  
acetylamino or hydroxy; and  
provided that when X is methylene,  
then both  $R^7$  and  $R^8$  are hydrogen.

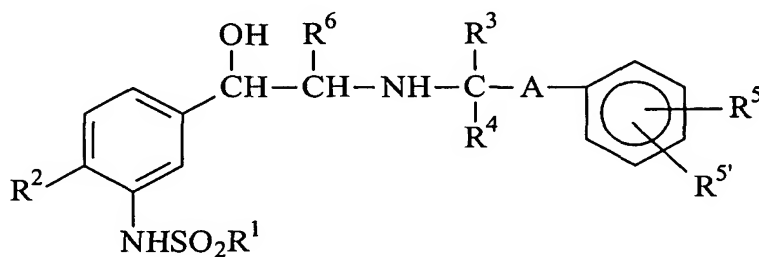
--17. (Twice amended) A method for the prophylactic and/or the therapeutic treatment of pollakiuria or urinary incontinence comprising administering to a subject in need thereof an effective amount of

[the compound as defined in Claim 10 or a pharmaceutically acceptable salt thereof]  
a compound, which is a  $\beta_3$  adrenergic receptor agonist, having a general formula selected from the group consisting of formula (IV), (V), (VI), (VII) and (VIII),  
or a salt or prodrug thereof, or for the compound of formula (VII) an ester or amide thereof;

wherein

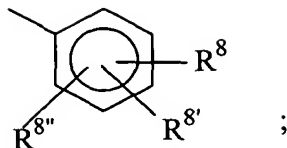
(a) a compound of formula (IV) is represented by the following general formula:

wherein



(IV)

$R^1$  is lower alkyl, aryl or arylalkyl;  
 $R^2$  is hydrogen, hydroxy, alkoxy,  $-\text{CH}_2\text{OH}$ , cyano,  $-\text{C}(\text{O})\text{OR}^7$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{CONH}_2$ ,  
tetrazole,  $-\text{CH}_2\text{NH}_2$  or halogen;  
 $R^3$  is hydrogen, alkyl, heterocycle or



$R^4$  is hydrogen, alkyl or B;

$R^5$ ,  $R^{5'}$ ,  $R^8$ ,  $R^{8'}$  and  $R^{8''}$  are independently hydrogen, alkoxy, lower alkyl, halogen, -OH, -CN,  $-(CH_2)_nNR^6COR^7$ ,  $-CON(R^6)R^{6'}$ ,  $-CON(R^6)OR^{6'}$ ,  $-CO_2R^6$ ,  $-SR^7$ ,  $-SOR^7$ ,  $-SO_2R^7$ ,  $-N(R^6)SO_2R^1$ ,  $-N(R^6)R^{6'}$ ,  $-NR^6COR^7$ ,  $-OCH_2CON(R^6)R^{6'}$ ,  $-OCH_2CO_2R^7$  or aryl; or

$R^5$  and  $R^{5'}$  or  $R^8$  and  $R^{8'}$  may together with the carbon atoms to which they are attached form an aryl or heterocycle;

$R^6$  and  $R^{6'}$  are independently hydrogen or lower alkyl; and

$R^7$  is lower alkyl;

$R^9$  and  $R^{9'}$  are independently hydrogen, lower alkyl, alkyl, cycloalkyl, arylalkyl, aryl, heteroaryl; or

$R^9$  and  $R^{9'}$  may together with the nitrogen atom to which they are attached form a heterocycle;

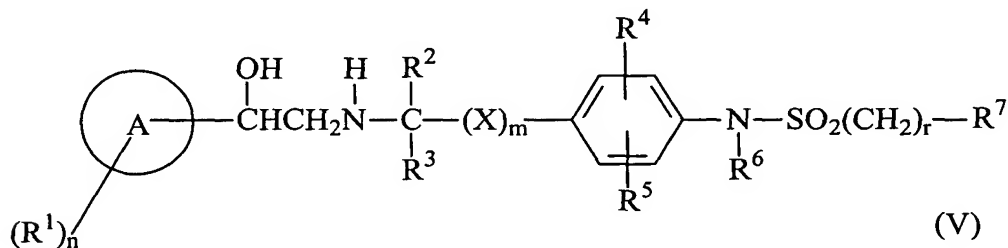
A is a bond,  $-(CH_2)_n-$  or  $-CH(B)-$ , wherein n is an integer of 1, 2 or 3 and

B is -CN,  $-CON(R^9)R^{9'}$  or  $-CO_2R^7$ ;

with the proviso that when A is a bond or  $-(CH_2)_n-$  and  $R^3$  is hydrogen or unsubstituted alkyl, then  $R^4$  is B or substituted alkyl;

(b) a compound of formula (V) is represented by the following general formula:

wherein



n is 0 to 5;

m is 0 or 1;

r is 0 to 3;

A is pyridinyl;

$R^1$  is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5)  $NR^8R^8$ , (6)  $SR^8$ , (7) trifluoromethyl, (8)  $C_1-C_{10}$  alkyl, (9)  $OR^8$ , (10)  $SO_2R^9$ , (11)  $OCOR^9$ , (12)  $NR^8COR^9$ , (13)  $COR^9$ , (14)  $NR^8SO_2R^9$ , (15)  $NR^8CO_2R^8$ , or (16)  $C_1-C_{10}$  alkyl substituted by hydroxy, halogen, cyano,  $NR^8R^8$ ,  $SR^8$ , trifluoromethyl,  $OR^8$ ,  $C_3-C_8$  cycloalkyl, phenyl,  $NR^8COR^9$ ,  $COR^9$ ,  $SO_2R^9$ ,  $OCOR^9$ ,  $NR^8SO_2R^9$  or  $NR^8CO_2R^8$ ;

$R^2$  and  $R^3$  are independently (1) hydrogen, (2)  $C_1-C_{10}$  alkyl or (3)  $C_1-C_{10}$  alkyl with 1 to 4 substituents selected from hydroxy,  $C_1-C_{10}$  alkoxy, or halogen;

$X$  is (1)  $-CH_2-$ , (2)  $-CH_2-CH_2-$ , (3)  $-CH=CH-$  or (4)  $-CH_2O-$ ;

$R^4$  and  $R^5$  are independently (1) hydrogen, (2)  $C_1-C_{10}$  alkyl, (3) halogen, (4)  $NHR^8$ , (5)  $OR^8$ , (6)  $SO_2R^9$  or (7)  $NHSO_2R^9$ ;

$R^6$  is (1) hydrogen or (2)  $C_1-C_{10}$  alkyl;

$R^7$  is  $Z-(R^{1a})_n$ ;

$R^{1a}$  is (1)  $R^1$ , (2)  $C_3-C_8$  cycloalkyl, (3) phenyl optionally substituted with up to 4 groups independently selected from  $R^8$ ,  $NR^8R^8$ ,  $OR^8$ ,  $SR^8$  or halogen, or (4) 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, optionally substituted with up to four groups independently selected from oxo,  $R^8$ ,  $NR^8R^8$ ,  $OR^8$ ,  $SR^8$ , or halogen;

$Z$  is (1) phenyl, (2) naphthyl, (3) or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (4) a benzene ring fused to a  $C_3-C_8$  cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a  $C_3-C_8$  cycloalkyl ring;

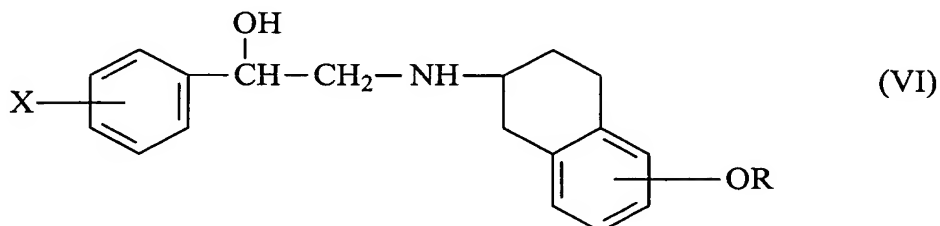
$R^8$  is (1) hydrogen, (2)  $C_1-C_{10}$ alkyl, (3)  $C_3-C_8$  cycloalkyl, (4)  $Z$  optionally having 1 to 4 substituents selected from halogen, nitro, oxo,  $NR^{10}R^{10}$ ,  $C_1-C_{10}$  alkyl,  $C_1-C_{10}$  alkoxy,  $C_1-C_{10}$  alkylthio, and  $C_1-C_{10}$  alkyl having 1 to 4 substituents selected from hydroxy, halogen,  $CO_2H$ ,  $CO_2-C_1-C_{10}$  alkyl,  $SO_2-C_1-C_{10}$  alkyl,  $C_3-C_8$  cycloalkyl,  $C_1-C_{10}$  alkoxy, or  $Z$  optionally substituted by from 1 to 3 halogen,  $C_1-C_{10}$  alkyl or  $C_1-C_{10}$  alkoxy, or (5)  $C_1-C_{10}$  alkyl having 1 to 4 substituents selected from hydroxy, halogen,  $CO_2H$ ,  $CO_2-C_1-C_{10}$  alkyl,  $SO_2-C_1-C_{10}$  alkyl,  $C_3-C_8$  cycloalkyl,  $C_1-C_{10}$  alkoxy,  $C_1-C_{10}$  alkyl, or  $Z$  optionally substituted by from 1 to 4 halogen,  $C_1-C_{10}$  alkyl or  $C_1-C_{10}$  alkoxy;



$R^9$  is (1)  $R^8$  or (2)  $NR^8R^8$ ; and

$R^{10}$  is (1)  $C_1$ - $C_{10}$  alkyl, or (2) two  $R^{10}$  groups together with the N to which they are attached forming a 5 or 6-membered ring optionally substituted with  $C_1$ - $C_{10}$  alkyl;

(c) a compound of formula (VI) is:

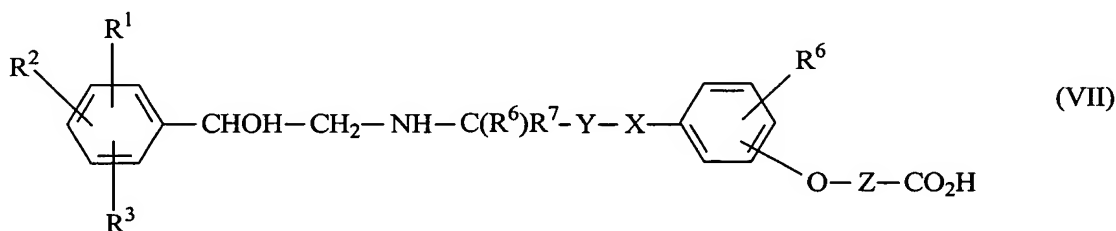


wherein

X is hydrogen, halogen, trifluoromethyl or lower alkyl, and

R is hydrogen; lower alkyl which may have a suitable substituent selected from the group consisting of cyclo( $C_3$ - $C_7$ )alkyl, hydroxy, lower alkoxy, carboxy and lower alkoxy carbonyl; cyclo( $C_3$ - $C_7$ )alkyl or lower alkanoyl;

(d) a compound of formula (VII) is represented by the following general formula:



wherein

$R^1$  is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or p-methoxybenzylamino group;

$R^2$  is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group;

$R^3$  is a hydrogen, chlorine or bromine atom or a hydroxyl group,

$R^4$  is a hydrogen atom or a methyl group;

$R^5$  is a hydrogen atom or a methyl group;

$R^6$  is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group;

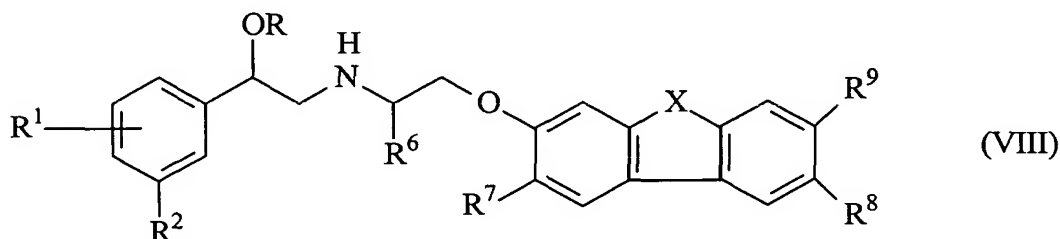


X is an oxygen atom or a bond;

Y is an alkylene group of up to 6 carbon atoms or a bond; and

Z is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms; and

(e) a compound of formula (VIII) is represented by the following general formula:



wherein

R is hydrogen or methyl,

R<sup>1</sup> is hydrogen, halogen, hydroxy, benzyloxy, amino or hydroxymethyl,

R<sup>2</sup> is hydrogen, hydroxymethyl, -NHR<sup>3</sup>, -SO<sub>2</sub>NR<sup>4</sup>R<sup>4'</sup> or nitro,

R<sup>3</sup> is hydrogen, methyl, -SO<sub>2</sub>R<sup>5</sup>, formyl or -CONHR<sup>6</sup>,

R<sup>4</sup> and R<sup>4'</sup> are independently hydrogen, lower alkyl or benzyl,

R<sup>5</sup> is lower alkyl, benzyl or -NR<sup>4</sup>R<sup>4'</sup>,

R<sup>6</sup> is hydrogen or lower alkyl,

R<sup>6'</sup> is hydrogen or lower alkyl,

R<sup>9</sup> is hydrogen, amino, acetylamino or hydroxy, and

X is N, O, S or methylene;

provided that when X is N, O or S,

then R<sup>9</sup> is hydrogen, either R<sup>7</sup> or R<sup>8</sup> is hydrogen, and the other is hydrogen, amino, acetylamino or hydroxy; and

provided that when X is methylene,

then both R<sup>7</sup> and R<sup>8</sup> are hydrogen.

18. (Twice amended) A method for the prophylactic and/or the therapeutic treatment of nervous pollakiuria, neurogenic bladder dysfunction, nocturia, unstable bladder, cystospasm, chronic cystitis, chronic prostatitis, overflow incontinence, passive incontinence, reflex incontinence, urge incontinence, urinary stress incontinence comprising administering to a subject in need thereof an effective amount of a compound,

[as defined in Claim 10 or a pharmaceutically acceptable salt thereof]

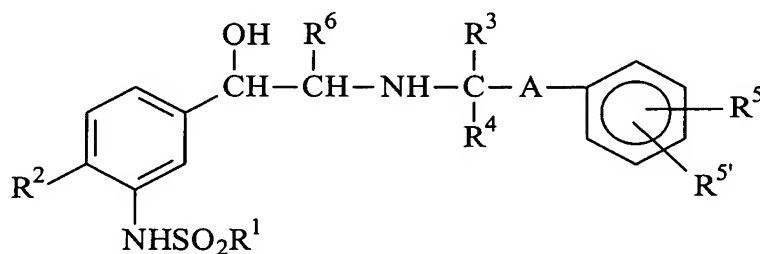
which is a  $\beta_3$  adrenergic receptor agonist, having a general formula selected from the group consisting of formula (IV), (V), (VI), (VII) and (VIII),

or a salt or prodrug thereof, or for the compound of formula (VII) an ester or amide thereof;

wherein

(a) a compound of formula (IV) is represented by the following general formula:

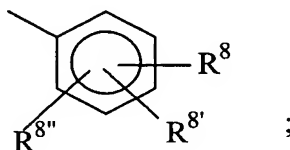
wherein



$R^1$  is lower alkyl, aryl or arylalkyl;

$R^2$  is hydrogen, hydroxy, alkoxy,  $-\text{CH}_2\text{OH}$ , cyano,  $-\text{C}(\text{O})\text{OR}^7$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{CONH}_2$ , tetrazole,  $-\text{CH}_2\text{NH}_2$  or halogen;

$R^3$  is hydrogen, alkyl, heterocycle or



$R^4$  is hydrogen, alkyl or B;

$R^5$ ,  $R^{5'}$ ,  $R^8$ ,  $R^{8'}$  and  $R^{8''}$  are independently hydrogen, alkoxy, lower alkyl, halogen,  $-\text{OH}$ ,  $-\text{CN}$ ,  $-(\text{CH}_2)_n\text{NR}^6\text{COR}^7$ ,  $-\text{CON}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{CON}(\text{R}^6)\text{OR}^{6'}$ ,  $-\text{CO}_2\text{R}^6$ ,  $-\text{SR}^7$ ,  $-\text{SOR}^7$ ,  $-\text{SO}_2\text{R}^7$ ,  $-\text{N}(\text{R}^6)\text{SO}_2\text{R}^1$ ,  $-\text{N}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{NR}^6\text{COR}^7$ ,  $-\text{OCH}_2\text{CON}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{OCH}_2\text{CO}_2\text{R}^7$  or aryl; or

$R^5$  and  $R^{5'}$  or  $R^8$  and  $R^{8'}$  may together with the carbon atoms to which they are attached form an aryl or heterocycle;

$R^6$  and  $R^{6'}$  are independently hydrogen or lower alkyl; and

$R^7$  is lower alkyl;

$R^9$  and  $R^{9'}$  are independently hydrogen, lower alkyl, alkyl, cycloalkyl, arylalkyl, aryl,

heteroaryl; or

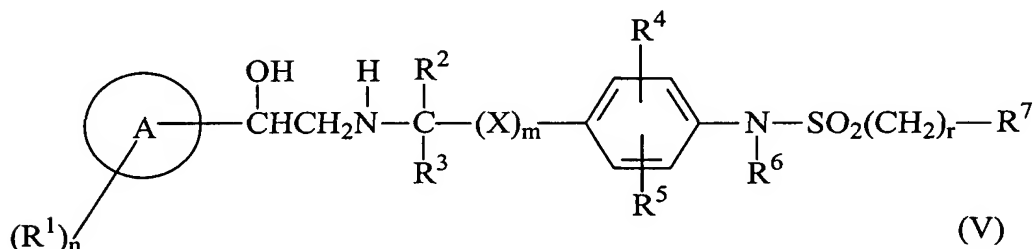
$R^9$  and  $R^{9'}$  may together with the nitrogen atom to which they are attached form a heterocycle;

A is a bond,  $-(CH_2)_n-$  or  $-CH(B)-$ , wherein n is an integer of 1, 2 or 3 and B is  $-CN$ ,  $-\text{CON}(R^9)R^{9'}$  or  $-\text{CO}_2R^7$ ;

with the proviso that when A is a bond or  $-(CH_2)_n-$  and  $R^3$  is hydrogen or unsubstituted alkyl, then  $R^4$  is B or substituted alkyl;

(b) a compound of formula (V) is represented by the following general formula:

wherein



n is 0 to 5;

m is 0 or 1;

r is 0 to 3;

A is pyridinyl;

$R^1$  is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5)  $\text{NR}^8\text{R}^8$ , (6)  $\text{SR}^8$ , (7) trifluoromethyl, (8)  $\text{C}_1\text{-C}_{10}$  alkyl, (9)  $\text{OR}^8$ , (10)  $\text{SO}_2\text{R}^9$ , (11)  $\text{OCOR}^9$ , (12)  $\text{NR}^8\text{COR}^9$ , (13)  $\text{COR}^9$ , (14)  $\text{NR}^8\text{SO}_2\text{R}^9$ , (15)  $\text{NR}^8\text{CO}_2\text{R}^8$ , or (16)  $\text{C}_1\text{-C}_{10}$  alkyl substituted by hydroxy, halogen, cyano,  $\text{NR}^8\text{R}^8$ ,  $\text{SR}^8$ , trifluoromethyl,  $\text{OR}^8$ ,  $\text{C}_3\text{-C}_8$  cycloalkyl, phenyl,  $\text{NR}^8\text{COR}^9$ ,  $\text{COR}^9$ ,  $\text{SO}_2\text{R}^9$ ,  $\text{OCOR}^9$ ,  $\text{NR}^8\text{SO}_2\text{R}^9$  or  $\text{NR}^8\text{CO}_2\text{R}^8$ ;

$R^2$  and  $R^3$  are independently (1) hydrogen, (2)  $\text{C}_1\text{-C}_{10}$  alkyl or (3)  $\text{C}_1\text{-C}_{10}$  alkyl with 1 to 4 substituents selected from hydroxy,  $\text{C}_1\text{-C}_{10}$  alkoxy, or halogen;

X is (1)  $-\text{CH}_2\text{CH}_2-$ , (2)  $-\text{CH}_2-$ , (3)  $-\text{CH}=\text{CH}-$  or (4)  $-\text{CH}_2\text{O}-$ ;

$R^4$  and  $R^5$  are independently (1) hydrogen, (2)  $\text{C}_1\text{-C}_{10}$  alkyl, (3) halogen, (4)  $\text{NHR}^8$ , (5)  $\text{OR}^8$ , (6)  $\text{SO}_2\text{R}^9$  or (7)  $\text{NHSO}_2\text{R}^9$ ;

$R^6$  is (1) hydrogen or (2)  $\text{C}_1\text{-C}_{10}$  alkyl;

$R^7$  is  $\text{Z}-(\text{R}^{1a})_n$ ;

$R^{1a}$  is (1)  $\text{R}^1$ , (2)  $\text{C}_3\text{-C}_8$  cycloalkyl, (3) phenyl optionally substituted with up to 4

groups independently selected from  $R^8$ ,  $NR^8R^8$ ,  $OR^8$ ,  $SR^8$  or halogen, or (4) 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, optionally substituted with up to four groups independently selected from oxo,  $R^8$ ,  $NR^8R^8$ ,  $OR^8$ ,  $SR^8$ , or halogen;

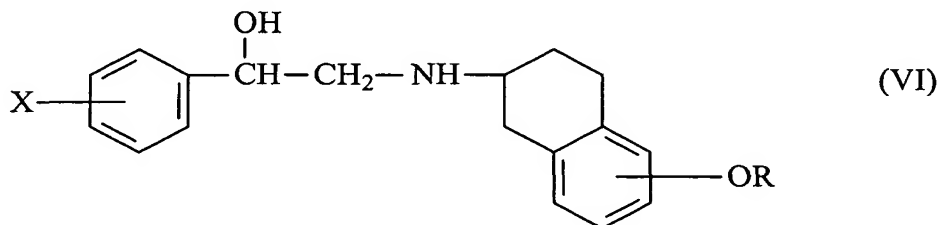
Z is (1) phenyl, (2) naphthyl, (3) or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (4) a benzene ring fused to a  $C_3$ - $C_8$  cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a  $C_3$ - $C_8$  cycloalkyl ring;

$R^8$  is (1) hydrogen, (2)  $C_1$ - $C_{10}$  alkyl, (3)  $C_3$ - $C_8$  cycloalkyl, (4) Z optionally having 1 to 4 substituents selected from halogen, nitro, oxo,  $NR^{10}R^{10}$ ,  $C_1$ - $C_{10}$  alkyl,  $C_1$ - $C_{10}$  alkoxy,  $C_1$ - $C_{10}$  alkylthio, and  $C_1$ - $C_{10}$  alkyl having 1 to 4 substituents selected from hydroxy, halogen,  $CO_2H$ ,  $CO_2$ - $C_1$ - $C_{10}$  alkyl,  $SO_2$ - $C_1$ - $C_{10}$  alkyl,  $C_3$ - $C_8$  cycloalkyl,  $C_1$ - $C_{10}$  alkoxy, or Z optionally substituted by from 1 to 3 halogen,  $C_1$ - $C_{10}$  alkyl or  $C_1$ - $C_{10}$  alkoxy, or (5)  $C_1$ - $C_{10}$  alkyl having 1 to 4 substituents selected from hydroxy, halogen,  $CO_2H$ ,  $CO_2$ - $C_1$ - $C_{10}$  alkyl,  $SO_2$ - $C_1$ - $C_{10}$  alkyl,  $C_3$ - $C_8$  cycloalkyl,  $C_1$ - $C_{10}$  alkoxy,  $C_1$ - $C_{10}$  alkyl, or Z optionally substituted by from 1 to 4 halogen,  $C_1$ - $C_{10}$  alkyl or  $C_1$ - $C_{10}$  alkoxy;

$R^9$  is (1)  $R^8$  or (2)  $NR^8R^8$ ; and

$R^{10}$  is (1)  $C_1$ - $C_{10}$  alkyl, or (2) two  $R^{10}$  groups together with the N to which they are attached forming a 5 or 6-membered ring optionally substituted with  $C_1$ - $C_{10}$  alkyl;

(c) a compound of formula (VI) is:

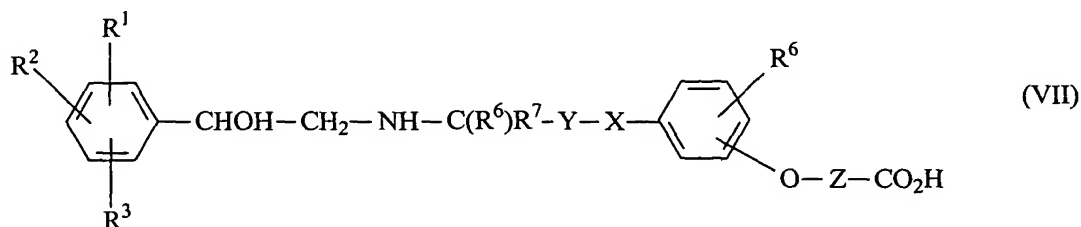


wherein

X is hydrogen, halogen, trifluoromethyl or lower alkyl, and

R is hydrogen; lower alkyl which may have a suitable substituent selected from the group consisting of cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl, hydroxy, lower alkoxy, carboxy and lower alkoxycarbonyl; cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl or lower alkanoyl;

(d) a compound of formula (VII) is represented by the following general formula:



wherein

R<sup>1</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or p-methoxybenzylamino group;

R<sup>2</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group;

R<sup>3</sup> is a hydrogen, chlorine or bromine atom or a hydroxyl group,

R<sup>4</sup> is a hydrogen atom or a methyl group;

R<sup>5</sup> is a hydrogen atom or a methyl group;

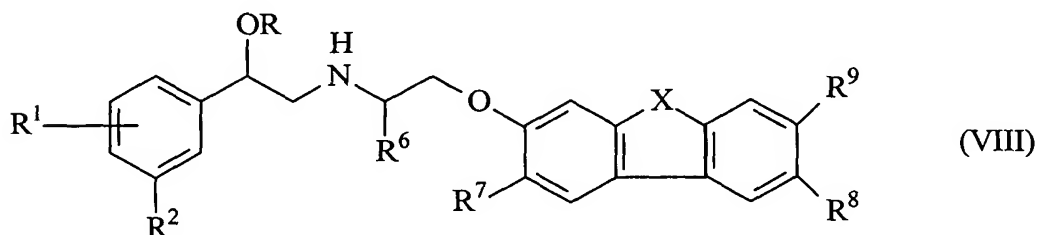
R<sup>6</sup> is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group;

X is an oxygen atom or a bond;

Y is an alkylene group of up to 6 carbon atoms or a bond; and

Z is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms; and

(e) a compound of formula (VIII) is represented by the following general formula:



wherein

R is hydrogen or methyl,

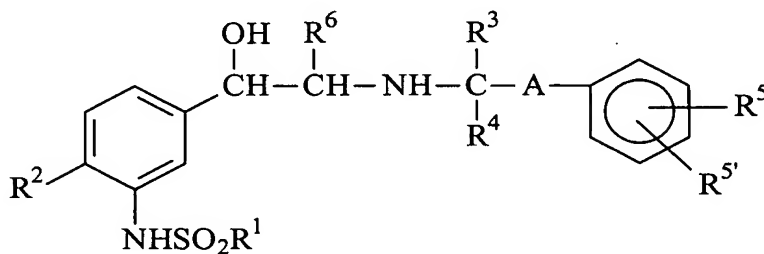
$R^1$  is hydrogen, halogen, hydroxy, benzyloxy, amino or hydroxymethyl,  
 $R^2$  is hydrogen, hydroxymethyl,  $-NHR^3$ ,  $-SO_2NR^4R^4$  or nitro,  
 $R^3$  is hydrogen, methyl,  $-SO_2R^5$ , formyl or  $-CONHR^6$ ,  
 $R^4$  and  $R^4$  are independently hydrogen, lower alkyl or benzyl,  
 $R^5$  is lower alkyl, benzyl or  $-NR^4R^4$ ,  
 $R^6$  is hydrogen or lower alkyl,  
 $R^6$  is hydrogen or lower alkyl,  
 $R^9$  is hydrogen, amino, acetylamino or hydroxy, and  
 $X$  is N, O, S or methylene;  
 provided that when  $X$  is N, O or S,  
 then  $R^9$  is hydrogen, either  $R^7$  or  $R^8$  is hydrogen, and the other is hydrogen, amino,  
 acetylamino or hydroxy; and  
 provided that when  $X$  is methylene,  
 then both  $R^7$  and  $R^8$  are hydrogen.

--19. (Twice amended) A commercial package comprising:  
 [the compound as defined in Claim 10]  
 a compound, which is a  $\beta_3$  adrenergic receptor agonist, having a general formula  
 selected from the group consisting of formula (IV), (V), (VI), (VII) and (VIII),  
 or a salt or prodrug thereof, or for the compound of formula (VII) an ester or amide  
 thereof;

wherein

(a) a compound of formula (IV) is represented by the following general formula:

wherein



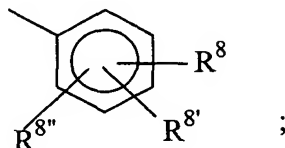
(IV)

$R^1$  is lower alkyl, aryl or arylalkyl;

$R^2$  is hydrogen, hydroxy, alkoxy,  $-CH_2OH$ , cyano,  $-C(O)OR^7$ ,  $-CO_2H$ ,  $-CONH_2$ ,

tetrazole,  $-\text{CH}_2\text{NH}_2$  or halogen;

$\text{R}^3$  is hydrogen, alkyl, heterocycle or



$\text{R}^4$  is hydrogen, alkyl or B;

$\text{R}^5$ ,  $\text{R}^{5'}$ ,  $\text{R}^8$ ,  $\text{R}^{8'}$  and  $\text{R}^{8''}$  are independently hydrogen, alkoxy, lower alkyl, halogen,  $-\text{OH}$ ,  $-\text{CN}$ ,  $-(\text{CH}_2)_n\text{NR}^6\text{COR}^7$ ,  $-\text{CON}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{CON}(\text{R}^6)\text{OR}^{6'}$ ,  $-\text{CO}_2\text{R}^6$ ,  $-\text{SR}^7$ ,  $-\text{SOR}^7$ ,  $-\text{SO}_2\text{R}^7$ ,  $-\text{N}(\text{R}^6)\text{SO}_2\text{R}^1$ ,  $-\text{N}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{NR}^6\text{COR}^7$ ,  $-\text{OCH}_2\text{CON}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{OCH}_2\text{CO}_2\text{R}^7$  or aryl; or

$\text{R}^5$  and  $\text{R}^{5'}$  or  $\text{R}^8$  and  $\text{R}^{8'}$  may together with the carbon atoms to which they are attached form an aryl or heterocycle;

$\text{R}^6$  and  $\text{R}^{6'}$  are independently hydrogen or lower alkyl; and

$\text{R}^7$  is lower alkyl;

$\text{R}^9$  and  $\text{R}^{9'}$  are independently hydrogen, lower alkyl, alkyl, cycloalkyl, arylalkyl, aryl, heteroaryl; or

$\text{R}^9$  and  $\text{R}^{9'}$  may together with the nitrogen atom to which they are attached form a heterocycle;

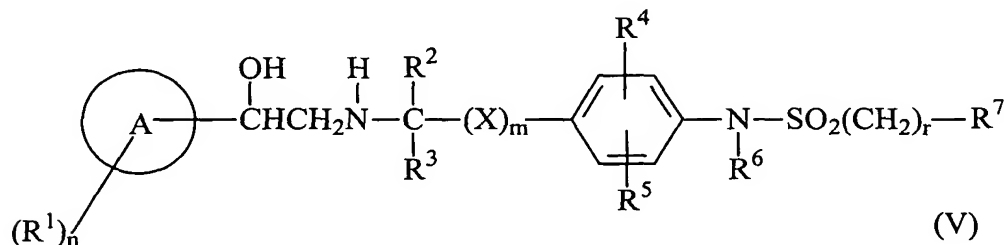
A is a bond,  $-(\text{CH}_2)_n-$  or  $-\text{CH}(\text{B})-$ , wherein n is an integer of 1, 2 or 3 and

B is  $-\text{CN}$ ,  $-\text{CON}(\text{R}^9)\text{R}^{9'}$  or  $-\text{CO}_2\text{R}^7$ ;

with the proviso that when A is a bond or  $-(\text{CH}_2)_n-$  and  $\text{R}^3$  is hydrogen or unsubstituted alkyl, then  $\text{R}^4$  is B or substituted alkyl;

(b) a compound of formula (V) is represented by the following general formula:

wherein



n is 0 to 5;

m is 0 or 1;

r is 0 to 3;

A is pyridinyl;

R<sup>1</sup> is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5) NR<sup>8</sup>R<sup>8</sup>, (6) SR<sup>8</sup>, (7) trifluoromethyl, (8) C<sub>1</sub>-C<sub>10</sub> alkyl, (9) OR<sup>8</sup>, (10) SO<sub>2</sub>R<sup>9</sup>, (11) OCOR<sup>9</sup>, (12) NR<sup>8</sup>COR<sup>9</sup>, (13) COR<sup>9</sup>, (14) NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup>, (15) NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>, or (16) C<sub>1</sub>-C<sub>10</sub> alkyl substituted by hydroxy, halogen, cyano, NR<sup>8</sup>R<sup>8</sup>, SR<sup>8</sup>, trifluoromethyl, OR<sup>8</sup>, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, NR<sup>8</sup>COR<sup>9</sup>, COR<sup>9</sup>, SO<sub>2</sub>R<sup>9</sup>, OCOR<sup>9</sup>, NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup> or NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>;

R<sup>2</sup> and R<sup>3</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl or (3) C<sub>1</sub>-C<sub>10</sub> alkyl with 1 to 4 substituents selected from hydroxy, C<sub>1</sub>-C<sub>10</sub> alkoxy, or halogen;

X is (1) -CH<sub>2</sub>-, (2) -CH<sub>2</sub>-CH<sub>2</sub>-, (3) -CH=CH- or (4) -CH<sub>2</sub>O-;

R<sup>4</sup> and R<sup>5</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl, (3) halogen, (4) NHR<sup>8</sup>, (5) OR<sup>8</sup>, (6) SO<sub>2</sub>R<sup>9</sup> or (7) NHSO<sub>2</sub>R<sup>9</sup>;

R<sup>6</sup> is (1) hydrogen or (2) C<sub>1</sub>-C<sub>10</sub> alkyl;

R<sup>7</sup> is Z-(R<sup>1a</sup>)<sub>n</sub>;

R<sup>1a</sup> is (1) R<sup>1</sup>, (2) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (3) phenyl optionally substituted with up to 4 groups independently selected from R<sup>8</sup>, NR<sup>8</sup>R<sup>8</sup>, OR<sup>8</sup>, SR<sup>8</sup> or halogen, or (4) 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, optionally substituted with up to four groups independently selected from oxo, R<sup>8</sup>, NR<sup>8</sup>R<sup>8</sup>, OR<sup>8</sup>, SR<sup>8</sup>, or halogen;

Z is (1) phenyl, (2) naphthyl, (3) or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (4) a benzene ring fused to a C<sub>3</sub>-C<sub>8</sub> cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a C<sub>3</sub>-C<sub>8</sub> cycloalkyl ring;

R<sup>8</sup> is (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub>alkyl, (3) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (4) Z optionally having 1 to 4 substituents selected from halogen, nitro, oxo, NR<sup>10</sup>R<sup>10</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>1</sub>-C<sub>10</sub> alkylthio, and C<sub>1</sub>-C<sub>10</sub> alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, SO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, or Z optionally substituted by from 1 to 3 halogen, C<sub>1</sub>-C<sub>10</sub> alkyl or C<sub>1</sub>-C<sub>10</sub> alkoxy, or (5) C<sub>1</sub>-C<sub>10</sub> alkyl having 1

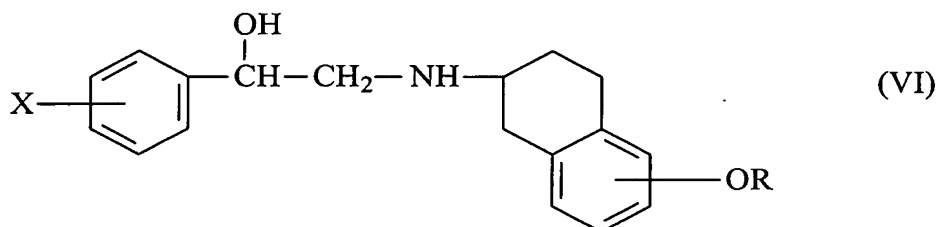


to 4 substituents selected from hydroxy, halogen,  $\text{CO}_2\text{H}$ ,  $\text{CO}_2\text{-C}_1\text{-C}_{10}$  alkyl,  $\text{SO}_2\text{-C}_1\text{-C}_{10}$  alkyl,  $\text{C}_3\text{-C}_8$  cycloalkyl,  $\text{C}_1\text{-C}_{10}$  alkoxy,  $\text{C}_1\text{-C}_{10}$  alkyl, or Z optionally substituted by from 1 to 4 halogen,  $\text{C}_1\text{-C}_{10}$  alkyl or  $\text{C}_1\text{-C}_{10}$  alkoxy;

$\text{R}^9$  is (1)  $\text{R}^8$  or (2)  $\text{NR}^8\text{R}^8$ ; and

$\text{R}^{10}$  is (1)  $\text{C}_1\text{-C}_{10}$  alkyl, or (2) two  $\text{R}^{10}$  groups together with the N to which they are attached forming a 5 or 6-membered ring optionally substituted with  $\text{C}_1\text{-C}_{10}$  alkyl;

(c) a compound of formula (VI) is:

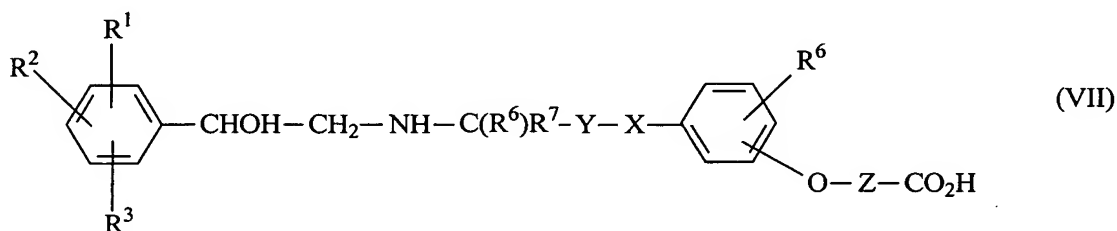


wherein

X is hydrogen, halogen, trifluoromethyl or lower alkyl, and

R is hydrogen; lower alkyl which may have a suitable substituent selected from the group consisting of cyclo( $\text{C}_3\text{-C}_7$ )alkyl, hydroxy, lower alkoxy, carboxy and lower alkoxycarbonyl; cyclo( $\text{C}_3\text{-C}_7$ )alkyl or lower alkanoyl;

(d) a compound of formula (VII) is represented by the following general formula:



wherein

$\text{R}^1$  is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or p-methoxybenzylamino group;

$\text{R}^2$  is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group;

$\text{R}^3$  is a hydrogen, chlorine or bromine atom or a hydroxyl group,

R<sup>4</sup> is a hydrogen atom or a methyl group;

R<sup>5</sup> is a hydrogen atom or a methyl group;

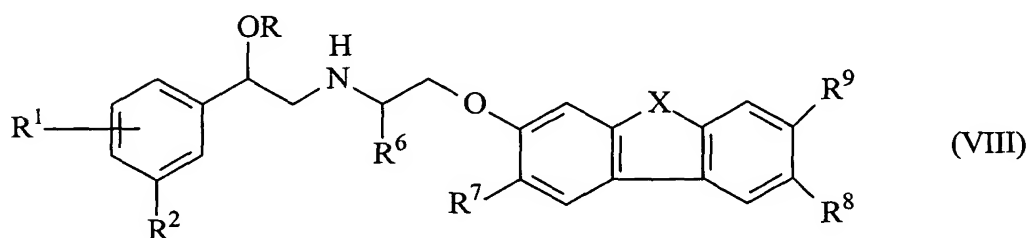
R<sup>6</sup> is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group;

X is an oxygen atom or a bond;

Y is an alkylene group of up to 6 carbon atoms or a bond; and

Z is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms; and

(e) a compound of formula (VIII) is represented by the following general formula:



wherein

R is hydrogen or methyl,

R<sup>1</sup> is hydrogen, halogen, hydroxy, benzyloxy, amino or hydroxymethyl,

R<sup>2</sup> is hydrogen, hydroxymethyl, -NHR<sup>3</sup>, -SO<sub>2</sub>NR<sup>4</sup>R<sup>4'</sup> or nitro,

R<sup>3</sup> is hydrogen, methyl, -SO<sub>2</sub>R<sup>5</sup>, formyl or -CONHR<sup>6'</sup>,

R<sup>4</sup> and R<sup>4'</sup> are independently hydrogen, lower alkyl or benzyl,

R<sup>5</sup> is lower alkyl, benzyl or -NR<sup>4</sup>R<sup>4'</sup>,

R<sup>6</sup> is hydrogen or lower alkyl,

R<sup>6'</sup> is hydrogen or lower alkyl,

R<sup>9</sup> is hydrogen, amino, acetylamino or hydroxy, and

X is N, O, S or methylene;

provided that when X is N, O or S,

then R<sup>9</sup> is hydrogen, either R<sup>7</sup> or R<sup>8</sup> is hydrogen, and the other is hydrogen, amino, acetylamino or hydroxy; and

provided that when X is methylene,

then both R<sup>7</sup> and R<sup>8</sup> are hydrogen.

and

written matter associated therewith,

wherein the written matter states that the pharmaceutical composition can or should

be used for preventing and/or treating dysuria.

20. (Twice amended) An article of manufacture comprising:

a packaging material and

the compound [as defined in Claim 10],

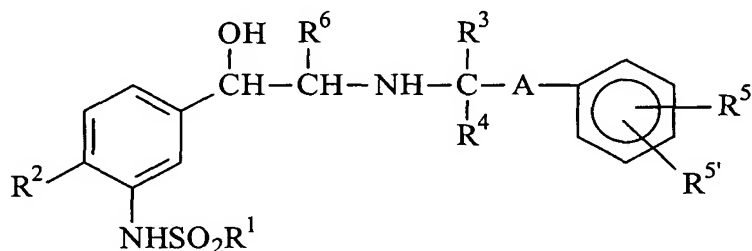
a compound, which is a  $\beta_3$  adrenergic receptor agonist, having a general formula selected from the group consisting of formula (IV), (V), (VI), (VII) and (VIII),

or a salt or prodrug thereof, or for the compound of formula (VII) an ester or amide thereof;

wherein

(a) a compound of formula (IV) is represented by the following general formula:

wherein

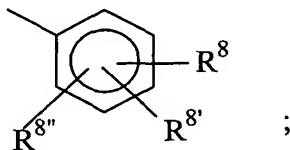


(IV)

$\text{R}^1$  is lower alkyl, aryl or arylalkyl;

$\text{R}^2$  is hydrogen, hydroxy, alkoxy,  $-\text{CH}_2\text{OH}$ , cyano,  $-\text{C}(\text{O})\text{OR}^7$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{CONH}_2$ , tetrazole,  $-\text{CH}_2\text{NH}_2$  or halogen;

$\text{R}^3$  is hydrogen, alkyl, heterocycle or



$\text{R}^4$  is hydrogen, alkyl or B;

$\text{R}^5$ ,  $\text{R}^{5'}$ ,  $\text{R}^8$ ,  $\text{R}^{8'}$  and  $\text{R}^{8''}$  are independently hydrogen, alkoxy, lower alkyl, halogen,  $-\text{OH}$ ,  $-\text{CN}$ ,  $-(\text{CH}_2)_n\text{NR}^6\text{COR}^7$ ,  $-\text{CON}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{CON}(\text{R}^6)\text{OR}^{6'}$ ,  $-\text{CO}_2\text{R}^6$ ,  $-\text{SR}^7$ ,  $-\text{SOR}^7$ ,  $-\text{SO}_2\text{R}^7$ ,  $-\text{N}(\text{R}^6)\text{SO}_2\text{R}^1$ ,  $-\text{N}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{NR}^6\text{COR}^7$ ,  $-\text{OCH}_2\text{CON}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{OCH}_2\text{CO}_2\text{R}^7$  or aryl; or

$\text{R}^5$  and  $\text{R}^{5'}$  or  $\text{R}^8$  and  $\text{R}^{8'}$  may together with the carbon atoms to which they are attached form an aryl or heterocycle;

R<sup>6</sup> and R<sup>6'</sup> are independently hydrogen or lower alkyl; and

R<sup>7</sup> is lower alkyl;

R<sup>9</sup> and R<sup>9'</sup> are independently hydrogen, lower alkyl, alkyl, cycloalkyl, arylalkyl, aryl, heteroaryl; or

R<sup>9</sup> and R<sup>9'</sup> may together with the nitrogen atom to which they are attached form a heterocycle;

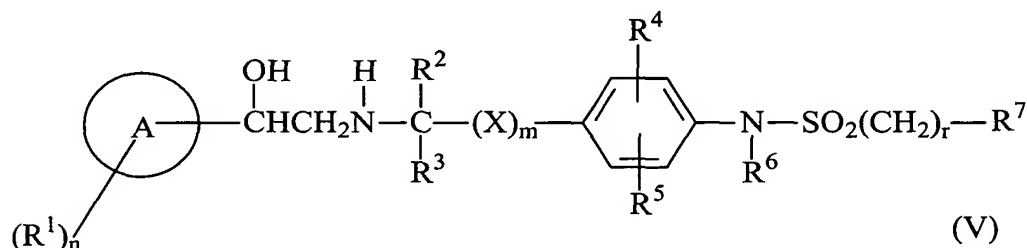
A is a bond, -(CH<sub>2</sub>)<sub>n</sub>- or -CH(B)-, wherein n is an integer of 1, 2 or 3 and

B is -CN, -CON(R<sup>9</sup>)R<sup>9'</sup>- or -CO<sub>2</sub>R<sup>7</sup>;

with the proviso that when A is a bond or -(CH<sub>2</sub>)<sub>n</sub>- and R<sup>3</sup> is hydrogen or unsubstituted alkyl, then R<sup>4</sup> is B or substituted alkyl;

(b) a compound of formula (V) is represented by the following general formula:

wherein



n is 0 to 5;

m is 0 or 1;

r is 0 to 3;

A is pyridinyl;

R<sup>1</sup> is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5) NR<sup>8</sup>R<sup>8</sup>, (6) SR<sup>8</sup>, (7) trifluoromethyl, (8) C<sub>1</sub>-C<sub>10</sub> alkyl, (9) OR<sup>8</sup>, (10) SO<sub>2</sub>R<sup>9</sup>, (11) OCOR<sup>9</sup>, (12) NR<sup>8</sup>COR<sup>9</sup>, (13) COR<sup>9</sup>, (14) NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup>, (15) NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>, or (16) C<sub>1</sub>-C<sub>10</sub> alkyl substituted by hydroxy, halogen, cyano, NR<sup>8</sup>R<sup>8</sup>, SR<sup>8</sup>, trifluoromethyl, OR<sup>8</sup>, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, NR<sup>8</sup>COR<sup>9</sup>, COR<sup>9</sup>, SO<sub>2</sub>R<sup>9</sup>, OCOR<sup>9</sup>, NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup> or NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>;

R<sup>2</sup> and R<sup>3</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl or (3) C<sub>1</sub>-C<sub>10</sub> alkyl with 1 to 4 substituents selected from hydroxy, C<sub>1</sub>-C<sub>10</sub> alkoxy, or halogen;

X is (1) -CH<sub>2</sub>-, (2) -CH<sub>2</sub>-CH<sub>2</sub>-, (3) -CH=CH- or (4) -CH<sub>2</sub>O-;

R<sup>4</sup> and R<sup>5</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl, (3) halogen, (4) NHR<sup>8</sup>, (5) OR<sup>8</sup>, (6) SO<sub>2</sub>R<sup>9</sup> or (7) NHSO<sub>2</sub>R<sup>9</sup>;

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$R^6$  is (1) hydrogen or (2)  $C_1$ - $C_{10}$  alkyl;

$R^7$  is  $Z-(R^{1a})_n$ ;

$R^{1a}$  is (1)  $R^1$ , (2)  $C_3$ - $C_8$  cycloalkyl, (3) phenyl optionally substituted with up to 4 groups independently selected from  $R^8$ ,  $NR^8R^8$ ,  $OR^8$ ,  $SR^8$  or halogen, or (4) 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, optionally substituted with up to four groups independently selected from oxo,  $R^8$ ,  $NR^8R^8$ ,  $OR^8$ ,  $SR^8$ , or halogen;

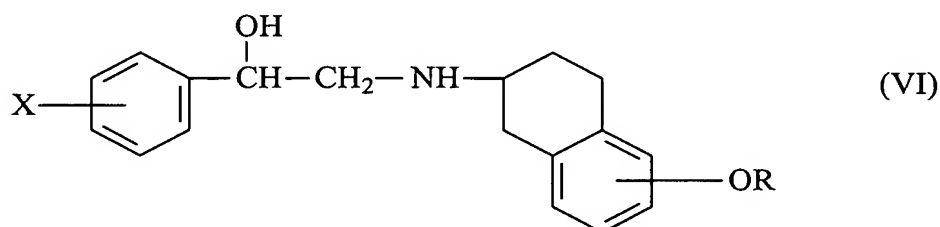
$Z$  is (1) phenyl, (2) naphthyl, (3) or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (4) a benzene ring fused to a  $C_3$ - $C_8$  cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a  $C_3$ - $C_8$  cycloalkyl ring;

$R^8$  is (1) hydrogen, (2)  $C_1$ - $C_{10}$ alkyl, (3)  $C_3$ - $C_8$  cycloalkyl, (4)  $Z$  optionally having 1 to 4 substituents selected from halogen, nitro, oxo,  $NR^{10}R^{10}$ ,  $C_1$ - $C_{10}$  alkyl,  $C_1$ - $C_{10}$  alkoxy,  $C_1$ - $C_{10}$  alkylthio, and  $C_1$ - $C_{10}$  alkyl having 1 to 4 substituents selected from hydroxy, halogen,  $CO_2H$ ,  $CO_2$ - $C_1$ - $C_{10}$  alkyl,  $SO_2$ - $C_1$ - $C_{10}$  alkyl,  $C_3$ - $C_8$  cycloalkyl,  $C_1$ - $C_{10}$  alkoxy, or  $Z$  optionally substituted by from 1 to 3 halogen,  $C_1$ - $C_{10}$  alkyl or  $C_1$ - $C_{10}$  alkoxy, or (5)  $C_1$ - $C_{10}$  alkyl having 1 to 4 substituents selected from hydroxy, halogen,  $CO_2H$ ,  $CO_2$ - $C_1$ - $C_{10}$  alkyl,  $SO_2$ - $C_1$ - $C_{10}$  alkyl,  $C_3$ - $C_8$  cycloalkyl,  $C_1$ - $C_{10}$  alkoxy,  $C_1$ - $C_{10}$  alkyl, or  $Z$  optionally substituted by from 1 to 4 halogen,  $C_1$ - $C_{10}$  alkyl or  $C_1$ - $C_{10}$  alkoxy;

$R^9$  is (1)  $R^8$  or (2)  $NR^8R^8$ ; and

$R^{10}$  is (1)  $C_1$ - $C_{10}$  alkyl, or (2) two  $R^{10}$  groups together with the N to which they are attached forming a 5 or 6-membered ring optionally substituted with  $C_1$ - $C_{10}$  alkyl;

(c) a compound of formula (VI) is:

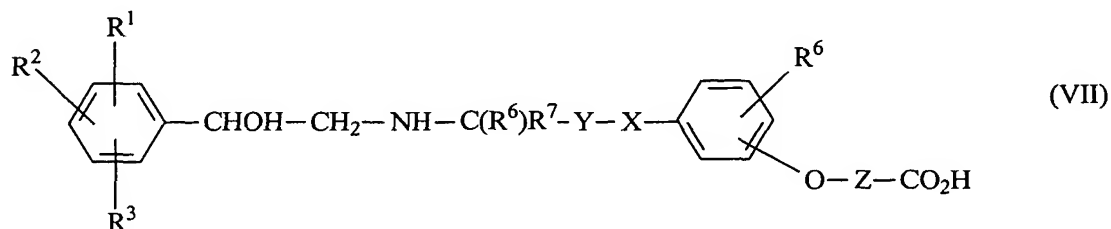


wherein

X is hydrogen, halogen, trifluoromethyl or lower alkyl, and

R is hydrogen; lower alkyl which may have a suitable substituent selected from the group consisting of cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl, hydroxy, lower alkoxy, carboxy and lower alkoxy carbonyl; cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl or lower alkanoyl;

(d) a compound of formula (VII) is represented by the following general formula:



wherein

R<sup>1</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or p-methoxybenzylamino group;

R<sup>2</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group;

R<sup>3</sup> is a hydrogen, chlorine or bromine atom or a hydroxyl group,

R<sup>4</sup> is a hydrogen atom or a methyl group;

R<sup>5</sup> is a hydrogen atom or a methyl group;

R<sup>6</sup> is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group;

X is an oxygen atom or a bond;

Y is an alkylene group of up to 6 carbon atoms or a bond; and

Z is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms; and

(e) a compound of formula (VIII) is represented by the following general formula:

